REMARKS

Restriction Requirement

The Examiner has required the Applicant to elect one of the following inventions for further examination: I. Claims 67, 69, 71 – 72, 77 – 84, 90 – 101, 106, 110 – 117, 120 – 122, drawn to nucleic acid compositions and methods of making said compositions, classified in class 514, and subclass 44; II. Claims 67 – 68, 70, 73 – 76, 85 – 105, 107, 120 – 122, drawn to polypeptide compositions and a method of making the polypeptides, classified in class 530, subclass 300; III. Claim 123, drawn to a method of vaccinating against Clostridium difficile, classified in class 424, subclass 247.1; IV. Claims 124 – 126, drawn to antibodies, classified in class 530, subclass 387.1.

Pursuant to the restriction requirement, Applicant elects the invention of Group I, Claims 67, 69, 71 – 72, 77 – 84, 89 (as amended), 90 – 101, 106, 110 – 117, 120 – 122, drawn to nucleic acid compositions and methods of making said compositions for further examination **with traverse**.

Applicant respectfully disagrees with the Examiner's distinction over the various invention Groups I to IV. The focus of the invention is a vaccine comprising *C. difficile* molecules which may be a *C. difficile* gene, *C. difficile* peptide/polypeptide or a derivative or fragment or mutant or variant thereof which is immunogenic in humans, or relevant antibodies. Applicant respectfully submits that Groups I, II and IV are closely related. An invention cannot have the peptides without the nucleic acids, or the antibodies without the peptides. An effective outcome of vaccination is generally related to a strong antibody response or in the case of a passive vaccine, to the provision of powerful opsonic antibodies. It would not be practical, or even possible, to manufacture the products separately. For example, peptides are generally produced from nucleic acids in live organisms by fermentation requiring either the native organism or a recombinant. Large quantities (typically hundreds of micrograms per individual) are required for immunizations. In order to develop an optimal immunisation procedure, it is necessary to

be able to produce a peptide- or DNA-based vaccine which may involve using different immunogens. Both DNA and peptide based vaccines essentially operate by generation of short peptide antigens in suitable cells, known as antigen presenting cells (APCs) which are then recognized by the effector T-cells of the immune system. In theory, with a DNA-based vaccine, the stronger emphasis is on stimulation of a cytolytic response, whereas with peptide-based vaccines, there is more emphasis on stimulation of antibody- and cytokine-mediated responses. The DNA in a vaccine is not active on its own, rather it must be transcribed and translated by the APC. Since there is difference in emphasis on the type of T-cell stimulated by DNA and peptide vaccines, there may be an advantage in alternating between DNA and peptide components for consecutive immunizations of one individual. Therefore, it may be found that optimal vaccination is achieved by administering a DNA vaccine for one injection and administering a peptide-based vaccine for subsequent immunization of the same individual, or vice versa.

In addition, the Examiner classified the peptides of the Group II inventions in class 530 and subclass 300. However, except for SEQ ID No. 1 and 2, all the other peptides are more than 100 amino acids long. A more appropriate classification should be class 530, subclass 350. In addition, Applicant respectfully submits that the amended Claim 89 from Group II should be incorporated into Group I. In summary, it is respectfully submitted that the restriction requirement should be withdrawn.

Election of Species Requirement

The Examiner has required the Applicant to elect a single disclosed species in Group I, if Group I is elected in the restriction requirement.

Pursuant to the requirement for election of species, Applicant elects SEQ ID NO. 4 for further examination **without traverse**. The claims readable on the elected species are Claims 78, 89, 111, and 122.

It is respectfully submitted that upon the allowance of the generic claims, Applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claims as provided by 37 CFR 1.141. In addition, it is believed that Applicant's teaching of equivalency in Applicant's own specification is not available to the Examiner as an admission in a rejection under 35 U.S.C. § 103. Any disclosure of equivalence in Applicant's specification cannot be used by the Examiner to support his/her rejection. See *In re Ruff et al.*, 256 F.2d. 590 (C.C.P.A. 1958).

OBJECTION TO SPECIFICATION:

The specification has been objected as containing certain informalities.

It is respectfully submitted that the relevant paragraph of the specification has been amended to delete the hyperlinks on page 10, line 9 and page 15, line 26 of the specification. In addition, Appendices 1 to 8 have been re-designated as Fig. 4 to 11, respectively (including Figs. 4A, 4B, 4C, 4D; 5A, 5B, 5C; 6A, 6B, 6C; 7A, 7B, 7C; 8A, 8B, 8C; 9A, 9B, 9C, 9D; 10A, 10B, 10C; 11A, 11B, 11C). The new sheets of the drawings have been provided. In addition, relevant references to the Appendices have been amended accordingly.

Therefore, the objection to the specification has been overcome and withdrawal of objection is respectfully requested.

SEQUENCE LISTNIGS:

Certain sequences appeared in the specification have not been listed in the Sequence Listing and submitted in a Computer Readable Format (CRF).

Applicant respectfully submits that the sequences appeared on page 16 lines 26 – 33 of the specification have been added to the modified Sequence Listing. In addition, the

amended Sequence Listing in CRF in a diskette has been submitted herewith. Please replace the originally filed "Sequence Listing" in paper copy and CRF with the currently enclosed "Sequence Listing" in paper copy and CRF.

According to the requirement of 37 CFR 1.821(f), Applicant hereby states that the information recorded in computer readable form is identical to the written listing of the paper copy currently submitted with the specification. In addition, Applicant hereby states that the submission, filed in accordance with 37 CFR 1.821(g), herein does not include new matter.

An action on the merits of all of the claims and a Notice of Allowance thereof are respectfully requested.

Respectfully submitted,

JACOBSON HOLMAN PLLC

By _____ Reg # 26421
John C. Holman
Registration No. 22,769

Date: July 28, 2005
(202) 638-6666
400 Seventh Street, N.W.
Washington, D.C. 20004
JCH/jc
Atty. Dkt. No.: P67635US0

Amendments to the Drawings:

The attached sheets of drawing include newly submitted Figs. 4A, 4B, 4C, 4D; 5A, 5B, 5C; 6A, 6B, 6C; 7A, 7B, 7C; 8A, 8B, 8C; 9A, 9B, 9C, 9D; 10A, 10B, 10C; 11A, 11B, 11C (collectively referred to as Figs. 4 – 11). The sheets containing Fig. 4 – 11, have been added to replace the Appendix 1 – 8 in the originally filed specification.

Attachment: Replacement Sheets (New Figures)